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510(k) SUMMARY

SUBMITTER:	Ortho Diagnostic Systems Inc. 1001 U.S. Hwy 202 Raritan, NJ 08869-0606	**CONTACT:** **Tel:** **Fax:**	Ms. Blanche Chien (908) 704-3920 (908) 218-8168
DEVICE NAME:	SynthAFax™ APTT Reagent	**PREDICATE:**	Activated THROMBOFAX® Reagent-Optimized
DATE:	December 8, 1995		

DEVICE DESCRIPTION:

SynthAFax APTT Reagent is a liquid buffered reagent which contains a blend of synthetic phospholipids formed in liposomes, and a soluble plasma activator, ellagic acid, for optimal activation of the contact phase of coagulation. The use of synthetic phospholipids assures uniformity in the reagent and lot-to-lot consistency.

The activated partial thromboplastin time (APTT) test uses an activating agent and a phospholipid source and calcium to optimally activate the intrinsic pathway of coagulation. SynthAFax is incubated with an anticoagulated plasma sample for a standard period of time, known as the contact activation time (CAT). SynthAFax initiates the contact phase of coagulation through the activation of Factor XII. The addition of calcium chloride allows for the binding of other coagulation factors to the phospholipid and subsequent activation of the coagulation cascade. The generation of thrombin eventually cleaves fibrinogen and activates Factor XIII which crosslinks the fibrin molecules to form a visible clot. This occurs within a specified period of time.

If there is a coagulation factor deficiency in the intrinsic pathway, the time required for the formation of the clot will be prolonged beyond that expected for normal plasma. There

will also be a prolongation of clotting caused by the presence of an inhibitor or the anticoagulant effect of heparin.

INTENDED USE:

SynthAFax APTT Reagent is intended for the two-stage activated partial thromboplastin time (APTT) test, specific factor assays, APTT substitution test and monitoring heparin therapy.

TECHNOLOGICAL CHARACTERISTICS:

Both SynthAFax APTT Reagent and the predicate, Activated THROMBOFAX are used for activated partial thromboplastin time determinations for which they are well correlated and have equivalent precision. Both reagents are sensitive to plasma coagulation Factors I, II, V, VIII, IX, X, XI, XII, Prekallikrein, Kininogen, and acquired factor deficiencies cause by disseminated intravascular coagulation and liver disease. Both reagents are equally sensitive to lupus anticoagulants and to the anticoagulant effects of heparin therapy.

SynthAFax APTT Reagent is prepared from synthetic phospholipids of a consistent fatty acid make up and a known amount of each type of phospholipid. Activated THROMBOFAX is prepared from a phospholipid mixture extracted from bovine brain tissue and has a variety of fatty acid chain lengths and proportion of unsaturation.

PERFORMANCE DATA:

Precision Study

The performance of SynthAFax APTT Reagent was evaluated at Ortho Diagnostic Systems, Inc., Raritan, NJ. The following data were derived from precision studies performed using both SynthAFax and Activated THROMBOFAX APTT Reagents and tested with ORTHO® Plasma Coagulation Control (OPCC) Level I (normal control), II and III (abnormal controls). The precision was tested on four different instruments to show the reagent equivalence independent of the instrument system.

TABLE 1: Precision Data

SynthAFax versus Activated THROMBOFAX APTT Reagent

OPCC Level I	Koagulab 60S		ELECTRA 1600		ELECTRA 1400		ELECTRA 1000	
	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.
Grand Mean (sec.) (n=180)	25.0	24.5	22.7	22.7	22.4	23.0	23.0	22.9
Replicate %CV (n=90)	0.9	0.5	0.8	0.4	0.7	0.5	0.8	0.5
Run to Run %CV (n=30)	0.8	1.2	0.6	0.6	0.8	1.0	0.8	0.8
Between Day %CV (n=5)	0.6	0.5	0.3	0.5	0.8	0.6	0.7	0.7

OPCC Level II	Koagulab 60S		ELECTRA 1600		ELECTRA 1400		ELECTRA 1000	
	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.
Grand Mean (sec.) (n=180)	41.4	46.6	36.2	40.5	36.0	41.6	36.5	40.5
Replicate %CV (n=90)	0.9	0.6	0.8	0.5	0.7	0.4	0.7	0.7
Run to Run %CV (n=30)	1.1	1.4	0.6	0.7	1.1	1.1	1.1	1.0
Between Day %CV (n=5)	0.8	1.2	0.4	0.5	1.1	0.7	0.8	0.8

OPCC Level III	Koagulab 60S		ELECTRA 1600		ELECTRA 1400		ELECTRA 1000	
	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.	SynthAFax	Act. Throm.
Grand Mean (sec.) (n=180)	54.5	61.9	47.9	53.4	47.2	53.4	46.9	54.3
Replicate %CV (n=90)	1.1	0.6	1.0	0.5	0.9	0.5	0.9	0.6
Run to Run %CV (n=30)	1.2	1.0	0.9	0.8	1.1	1.0	1.3	0.9
Between Day %CV (n=5)	0.9	0.9	0.7	0.5	1.1	0.6	1.0	0.8

Reagent Correlation Study

A total of one hundred (100) fresh normal donor plasma samples and seventy nine (79) frozen abnormal plasma samples from forty one (41) patients on heparin therapy, eleven (11) patients on oral anticoagulant therapy, three (3) patients with liver disease, and twenty four (24) lupus anticoagulant patients were tested for APTT with both SynthAFax and Activated THROMBOFAX APTT Reagents, using the KoaguLab 60-S Coagulation System and the ELECTRA 1600C. Data are shown in Figures 1 and 2 on the following page. For the KoaguLab 60-S, the correlation coefficient was 0.951, indicating acceptable correlation between the two reagents. The slope of the regression line was 1.08 indicating slightly more sensitivity for SynthAFax as compared to Activated THROMBOFAX APTT reagent. Similar results were seen on the ELECTRA 1600C.

Data From Reagent Correlation Studies

Figure 1: Correlation Studies
Koagulab 60-S

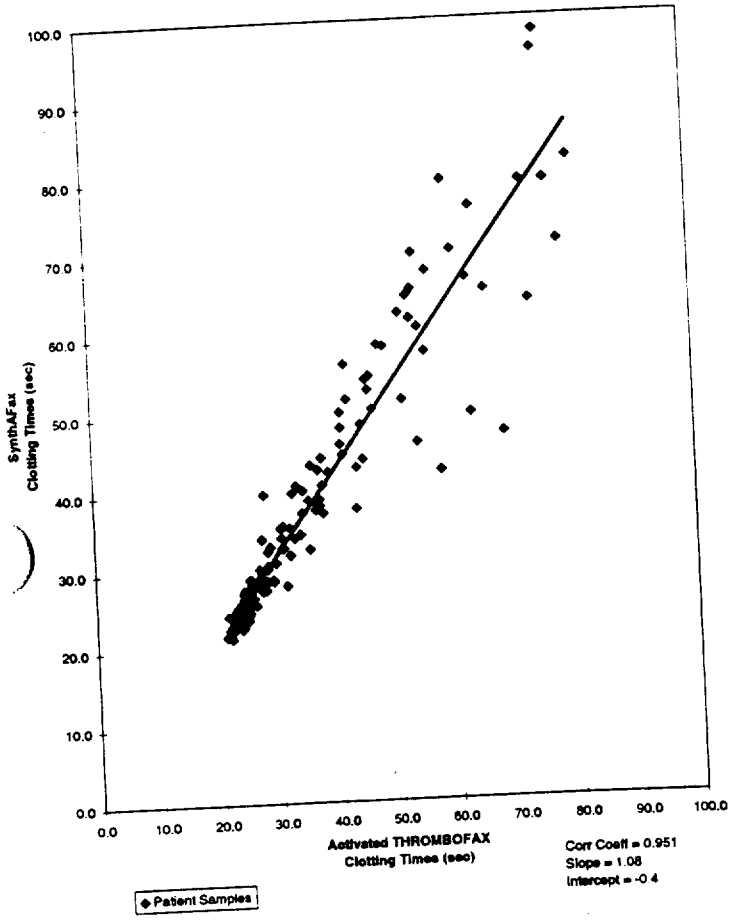
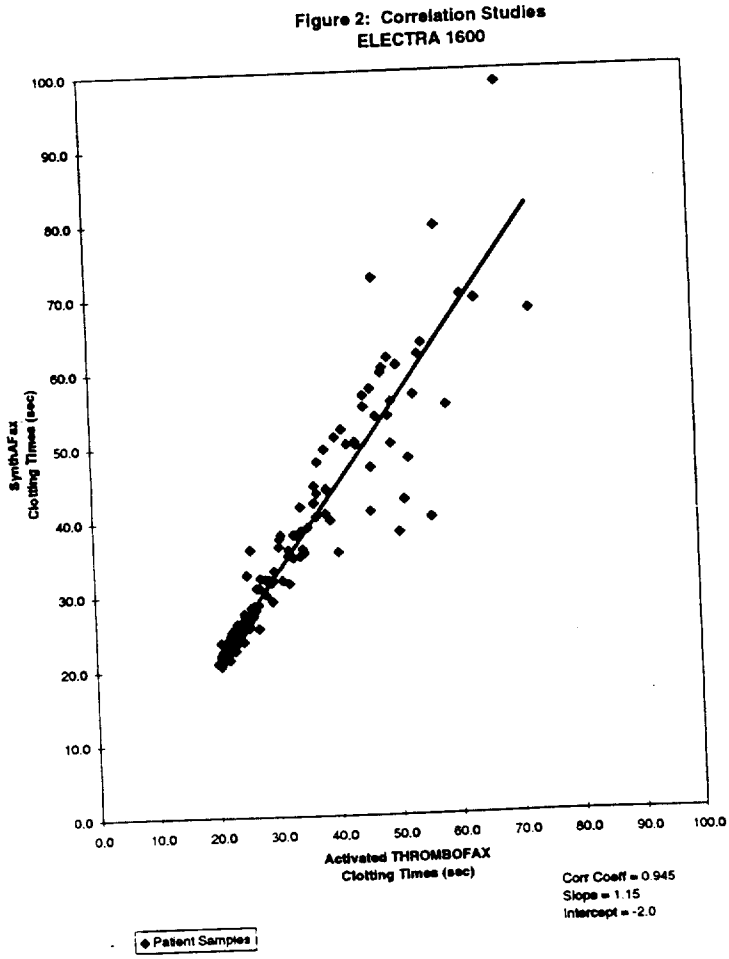


Figure 2: Correlation Studies
ELECTRA 1600



Factor Assay Standard Curves

Factor VIII, IX, XI and XII Assay Standard Curves were performed with SynthAFax and Activated THROMBOFAX APTT Reagents on both the KoaguLab 60-S Coagulation System and ELECTRA 1600C. On the KoaguLab 60-S, the factor curve responsiveness was equivalent for Factors VIII, IX, XI, and XII compared to Activated THROMBOFAX, and all standard curves had correlation coefficients of 0.986 or better, indicating acceptable correlation. Factor curves on the ELECTRA 1600C analyzer were fit with third order polynomial regressions and all gave correlation coefficients of 0.995 or better.

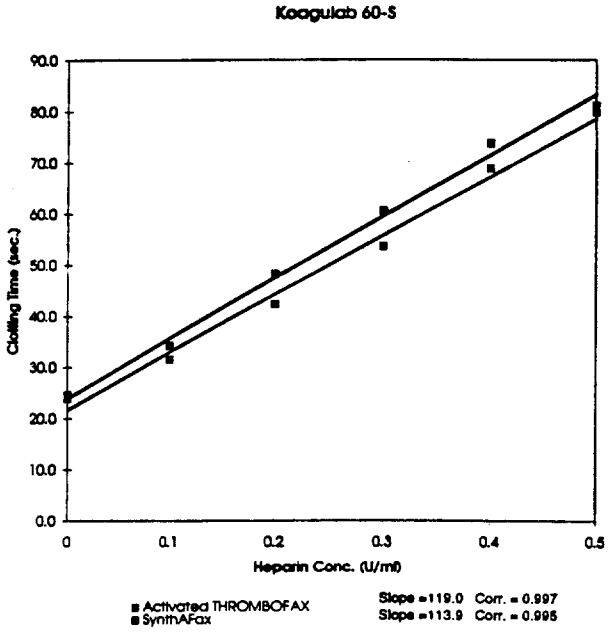
Data From Factor Assay Standard Curves

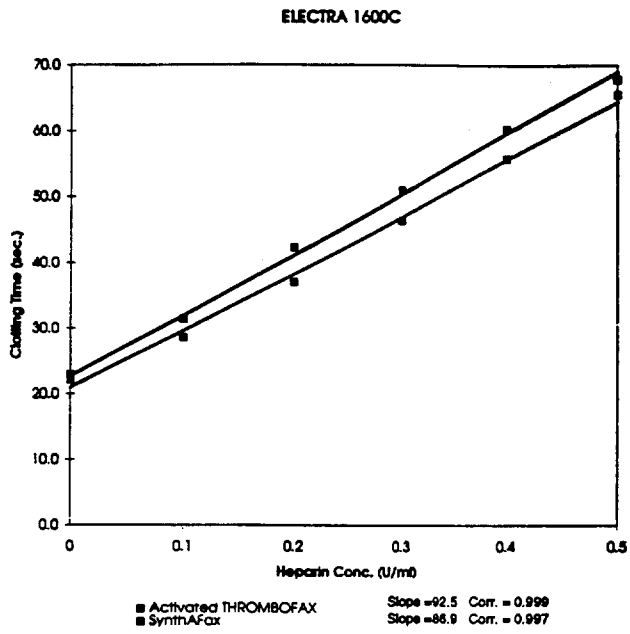
	Koagulab 60-S		ELECTRA 1600C	
	ORTHO SynthAFax	Activated THROMBOFAX	ORTHO SynthAFax	Activated THROMBOFAX
Factor VIII				
Slope	-0.130	-0.108		
Y-Intercept	1.823	1.829		
Corr. Coef.	0.988	0.995	1.000	0.997
Factor IX				
Slope	-0.129	-0.104		
Y-Intercept	1.803	1.820		
Corr. Coef.	0.994	0.986	1.000	0.998
Factor XI				
Slope	-0.173	-0.173		
Y-Intercept	1.996	1.996		
Corr. Coef.	0.997	0.995	0.997	0.995
Factor XII				
Slope	-0.239	-0.288		
Y-Intercept	2.021	2.215		
Corr. Coef.	0.994	0.995	0.999	0.998

In Vitro Heparin Sensitivity

The in vitro heparin sensitivity for SynthAFax and Activated THROMBOFAX APTT reagents was determined by performing a heparin response curve on the KoaguLab 60-S and ELECTRA 1600C using heparinized plasma dilutions at 0 to 0.5 units/ml. Heparin was added at the appropriate levels to a fresh normal plasma pool consisting of 10 normal donors. The slopes of the in vitro heparin response curve were equivalent for SynthAFax (113.9) and Activated THROMBOFAX (119.0) on the Koagulab 60-S, indicating equivalent sensitivity to heparinized plasma samples. On the ELECTRA 1600C the slopes were also equivalent for SynthAFax (86.9) and Activated THROMBOFAX (92.5)

In Vitro Heparin Curves





CONCLUSION

SynthAFax APTT Reagent is substantially equivalent to Activated THROMBOFAX Reagent-Optimized currently in commercial distribution by Ortho Diagnostic Systems Inc. as an activated partial thromboplastin time reagent used to determine deficiencies of clotting factor activity, either hereditary or acquired, in the intrinsic coagulation pathway or to monitor the effect of anticoagulant therapy.